Remarks

New claims 52-77 are added. Support for these claims can be found throughout the specification. Because applicants are suggesting an interference, they will discuss the specific support for the new claims in the claim charts provided below pursuant to 37 C.F.R. § 41.202(a)(5).

Applicants have cancelled claims 37-51 to expedite declaration of an interference. Applicants reserve the right to present claims to the cancelled subject matter in this or another application at a later date.

§ 41.202(a)(1)

Applicants seek an interference with U.S. Patent No. 6,693,086 ("the '086 patent"), which issued on February 17, 2004.

§ 41.202(a)(2)

Applicants believe all the claims of the '086 patent (claims 1-18) interfere with all the pending claims in the present application (claims 52-77). Specifically, Applicants believe that composition claims 1-9 of the '086 patent interfere with composition claims 52-64 of the present application and that method claims 10-18 of the '086 patent interfere with method claims 65-77 of the present application.

Applicants propose two counts:

count 1: the composition of claim 1 of the '086 patent

or

the composition of claim 52 of the present application; and

count 2: the method of claim 10 of the '086 patent

or

the method of claim 65 of the present application.

The counts recite specific claims, and the recited claims are the only independent claims. Accordingly, claims 1-9 of the '086 patent and claims 52-64 of the present application

correspond to count 1, and claims 10-18 of the '086 patent and claims 65-77 of the present application correspond to count 2.

For the Examiner's convenience, Applicants file herewith two suggested Interference Initial Memoranda (Form PTO-850) setting forth this information for each count.

§ 41.202(a)(3)

The following two claim charts compare the independent claims of the two parties for each of the two counts.

Count 1

Claim 52 filed herewith	Claim 1 of US 6,693,086 B1
A composition for activating a non-specific immune response in a subject comprising	A composition for the elicitation of a systemic, non-antigen specific immune response in a mammal, comprising:
an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains . . . a lipid or a sterol, wherein the lipid is a cationic lipid, virosome or liposome,	a. a cationic liposome delivery vehicle; and
an immunostimulatory CpG containing oligonucleotide associated with [1]	b. an isolated nucleic acid molecule selected from the group consisting of: i. an oligonucleotide comprising a CpG motif; and ii. an isolated bacterially-derived nucleic acid vector without a gene insert, or a fragment thereof;
wherein the composition activates a systemic, non-specific immune response in the subject.	wherein said therapeutic composition elicits a systemic, non-antigen-specific immune response in said mammal.

[1] This phrase actually appears in the ellipsis above. Applicants place it here in the claim chart for ease of comparison.

Count 2

Claim 65 filed herewith	Claim 10 of US 6,693,086 B1
A method for activating a non-specific immune response in a subject comprising	A method for eliciting of a systemic, non-antigen specific immune response in a mammal, comprising:
administering to a subject a composition comprising an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains . . . a lipid or a sterol, wherein the lipid is a cationic lipid, virosome or liposome,	administering to said mammal an amount of a composition effective to elicit said immune response, wherein said composition comprises: a. a cationic liposome delivery vehicle; and
an immunostimulatory CpG containing oligonucleotide associated with[2]	b. an isolated nucleic acid molecule selected from the group consisting of: i. an oligonucleotide comprising a CpG motif; and ii. an isolated bacterially-derived nucleic acid vector without a gene insert, or a fragment thereof.

Applicants note that, while the claims of the '086 patent recite "systemic," applicants' claims do not. This additional word in the claims of the '086 patent does not prevent them from interfering with the claims of the present application. For example, nothing contained in the body of claim 1 of the '086 patent would cause the composition to necessarily produce only a "systemic" response. Rather, the '086 patent teaches that the generation of a systemic response is dependent upon the route of administration: "alternate, non-systemic routes of administration (i.e., other than intravenous or intraperitoneal)." [Col. 10, lines 64-66.] Thus, intravenous or intraperitoneal administration results in a systemic response. [Col. 33, lines 39-47 ("[A]dministration of the nucleic acid:lipid complexes can be at any site in the mammal wherein systemic administration (i.e., intravenous or intraperitoneal administration) is possible.").]

Applicants' dependent claims 64 and 77 recite intravenous and intraperitoneal administration of the composition. As the '086 patent indicates, such administration routes would result in a systemic immune response.

[2] This phrase actally appears in the ellipsis above. Applicants place it here in the claim chart for ease of comparison.

As can be seen from the above claim charts, if they had been available as prior art, claims 1-9 of the '086 patent would have anticipated or rendered obvious claims 52-64 of the present application, and vice versa. *See* § 41.203(a). Thus, these claim sets, which applicants propose be designated as corresponding to count 1, interfere with each other.

Similarly, if they had been available as prior art, claims 10-18 of the '086 patent would have anticipated or rendered obvious claims 65-77 of the present application, and vice versa. *See* § 41.203(a). Thus, these claim sets, which applicants propose be designated as corresponding to count 2, also interfere with each other.

Applicants note that counts must be patentably distinct, but the test for patentable distinctness is a one-way test, not a two-way test. Final Rule, 69 Fed. Reg. 49960, 49991. col. 1 (August 12, 2004). Because the composition of count 1 would not necessarily anticipate or render obvious the method of count 2, an interference should be declared with two counts.

§ 41.202(a)(4)

The '086 patent issued from an application filed on June 25, 1998 and does not contain any priority claim.

The present application claims priority (via application Serial No. 09/415,142) to application Serial No. 08/386,063, filed February 7, 1995. Because those applications are related as continuations, applicants are entitled to priority as of the February 7, 1995 date. Because applicants are entitled to a date of at least over two years before the '086 patent is, applicants will prevail on priority.

Indeed, as applicants show in the claim chart below, they are also entitled to priority from application Serial No. 08/276,358, filed on July 15, 1994. Accordingly, applicants are entitled to a priority date that is almost four years before the priority date of the '086 patent, and applicants will prevail on priority.

§ 41.202(a)(5)

The following charts of the claims filed herewith show the written description of each new claim. Because there are two independent claims with identical pairs of dependent claims, applicants will first provide charts for the two independent claims, followed by charts for each pair of the dependent claims.

New Claim Number	Support in Specification
52. A composition for activating	The instant invention is based on the finding that certain oligonucleotides containing unmethylated cytosine-guanine (CpG) dinucleotides activate lymphocytes as evidenced by in vitro and in vivo data. Based on this finding, the invention features, in one aspect, novel immunostimulatory oligonucleotide compositions. [Page 7, lines 7-10.] Activated lymphocytes, stimulated by the methods described herein (e.g. either ex vivo or in vivo), can boost a subject's immune response. [Page 7, lines 33-35.] [Claim] 17. A method for treating, preventing or ameliorating an immune system deficiency in a subject comprising the steps of : a) contacting lymphocytes obtained from the subject with a composition of claim 1 ex vivo, thereby producing activated lymphocytes; and b) readministering the activated lymphocytes obtained in step a) to the subject. [Page 40, lines 26-34.]
non-specific immune response in a subject comprising:	The studies reported above indicate that unmethylated CpG containing oligonucleotides are directly mitogenic for lymphocytes (e.g. B cells and NK cells). [Page 23, lines 4-5.] This novel activation pathway provides a rapid **alternative to** T cell dependent antigen **specific** B cell activation. However, it is likely that B cell activation **would not be totally nonspecific**. [Page 23, lines 13-15 (emphasis added).] Further, sepsis, which is characterized by high morbidity and mortality due to massive and **nonspecific activation** of the immune system may be initiated by bacterial DNA and other products released from dying bacteria that reach concentrations sufficient to directly activate many lymphocytes. [Page 23, lines 33-36.]

an oligonucleotide delivery complex,	An "oligonucleotide delivery complex" shall mean an oligonucleotide associated with (e.g. ionically or covalently bound to; or encapsulated within) a targeting means (e.g. a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells). [Page 11, lines 10-13.] For administration in vivo, oligonucleotides may be associated with a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells to form an "oligonucleotide delivery complex". [Page 20, line 33-36.]
wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide	The instant invention is based on the finding that certain oligonucleotides containing unmethylated cytosine-guanine (CpG) dinucleotides activate lymphocytes as evidenced by in vitro and in vivo data. Based on this finding, the invention features, in one aspect, novel immunostimulatory oligonucleotide compositions. [Page 7, lines 7-10.] An "immunostimulatory oligonucleotide", "immunostimulatory CpG containing oligonucleotide", or "CpG ODN" refer to an oligonucleotide, which contains a cytosine, guanine dinucleotide sequence and stimulates (e.g. has a mitogenic effect) on vertebrate lymphocyte. [Page 10, lines 1-4.]
associated with a lipid or a sterol, wherein the lipid is a cationic lipid, virosome or liposome,	An "oligonucleotide delivery complex" shall mean an oligonucleotide associated with (e.g. ionically or covalently bound to; or encapsulated within) a targeting means (e.g. a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells). Examples of oligonucleotide delivery complexes include oligonucleotides associated with: a sterol (e.g. cholesterol), a lipid (e.g. a cationic lipid, virosome or liposome), or a target cell specific binding agent (e.g. a ligand recognized by

	target cell specific receptor). [Page 11, lines 10-16.] For administration in vivo, oligonucleotides may be associated with a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells to form an "oligonucleotide delivery complex". Oligonucleotides can be ionically, or covalently associated with appropriate molecules using techniques which are well known in the art. A variety of coupling or crosslinking agents can be used e.g. protein A, carbodiimide, and N-succinimidyl-3-(2-pyridyldithio) propionate (SPDP). Oligonucleotides can alternatively be encapsulated in liposomes or virosomes using well-known techniques. [Page 20, line 33, through page 21, line 2.]
wherein the composition activates a non-specific immune response in the subject.	The immunostimulatory oligonucleotides can therefore be used to treat, prevent or ameliorate an immune system deficiency (e.g., a tumor or cancer or a viral, fungal, bacterial or parasitic infection) in a subject. [Page 7, lines 35-37.] An "immune system deficiency" shall mean a disease or disorder in which the subject's immune system is not functioning in normal capacity or in which it would be useful to boost a subject's immune response for example to eliminate a tumor or cancer . . . or a viral . . . , fungal . . . , bacterial or parasitic . . . infection in a subject. [Page 11, lines 21-26.] Based on their immunostimulatory properties, oligonucleotides containing at least one unmethylated CpG dinucleotide can be administered to a subject in vivo to treat an "immune system deficiency". Alternatively, oligonucleotides containing at least one unmethylated CpG dinucleotide can be contacted with lymphocytes (e.g. B cells or NK cells) obtained from a subject having an immune system deficiency ex vivo and activated lymphocytes can then be reimplanted

	in the subject. [Page 21, lines 11-16.] An "immune system deficiency" shall mean a disease or disorder in which the subject's immune system is not functioning in normal capacity or in which it would be useful to boost a subject's immune response for example to eliminate a tumor or cancer . . . or a viral . . . , fungal . . . , bacterial or parasitic . . . infection in a subject. [Page 11, lines 21-26.] The studies reported above indicate that unmethylated CpG containing oligonucleotides are directly mitogenic for lymphocytes (e.g. B cells and NK cells). [Page 23, lines 4-5.] This novel activation pathway provides a rapid **alternative to** T cell dependent antigen **specific** B cell activation. However, it is likely that B cell activation **would not be totally nonspecific**. [Page 23, lines 13-15 (emphasis added).] For example, autoimmune responses to self antigens would also tend to be preferentially triggered by bacterial infections, since autoantigens could also provide a second activation signal to **autoreactive B cells triggered by bacterial DNA**. Indeed the induction of autoimmunity by bacterial infections is a common clinical observance. [Page 23, lines 21-25 (emphasis added).] Further, sepsis, which is characterized by high morbidity and mortality due to massive and **nonspecific activation** of the immune system may be initiated by bacterial DNA and other products released from dying bacteria that reach concentrations sufficient to directly activate many lymphocytes. [Page 23, lines 33-36.]
65. A method for activating	The instant invention is based on the finding that certain oligonucleotides containing unmethylated cytosine-guanine (CpG) dinucleotides activate lymphocytes as evidenced by in vitro and in vivo data. Based

	on this finding, the invention features, in one aspect, novel immunostimulatory oligonucleotide compositions. [Page 7, lines 7-10.] Activated lymphocytes, stimulated by the methods described herein (e.g. either ex vivo or in vivo), can boost a subject's immune response. [Page 7, lines 33-35.] [Claim] 17. A method for treating, preventing or ameliorating an immune system deficiency in a subject comprising the steps of : a) contacting lymphocytes obtained from the subject with a composition of claim 1 ex vivo, thereby producing activated lymphocytes; and b) readministering the activated lymphocytes obtained in step a) to the subject. [Page 40, lines 26-34.]
	The immune system may have evolved ways to preferentially respond to microbial nucleic acids. [Page 3, lines 11-13.] The immunostimulatory oligonucleotides can therefore be used to treat, prevent or ameliorate an immune system deficiency (e.g., a tumor or cancer or a viral, fungal, bacterial or parasitic infection) in a subject. [Page 7, lines 35-37.] An "immune system deficiency" shall mean a disease or disorder in which the subject's immune system is not functioning in normal capacity or in which it would be useful to boost a subject's immune response for example to eliminate a tumor or cancer . . . or a viral . . . , fungal . . . , bacterial or parasitic . . . infection in a subject. [Page 11, lines 21-26.] Based on their immunostimulatory properties, oligonucleotides containing at least one unmethylated CpG dinucleotide can be administered to a subject in vivo to treat an "immune system deficiency". Alternatively, oligonucleotides containing at least one unmethylated CpG dinucleotide can be contacted with lymphocytes (e.g. B cells or NK

	cells) obtained from a subject having an immune system deficiency ex vivo and activated lymphocytes can then be reimplanted in the subject. [Page 21, lines 11-16.]
non-specific immune response in a subject comprising: administering to a subject a composition comprising	The studies reported above indicate that unmethylated CpG containing oligonucleotides are directly mitogenic for lymphocytes (e.g. B cells and NK cells). [Page 23, lines 4-5.] This novel activation pathway provides a rapid **alternative to** T cell dependent antigen **specific** B cell activation. However, it is likely that B cell activation **would not be totally nonspecific**. [Page 23, lines 13-15 (emphasis added).] Further, sepsis, which is characterized by high morbidity and mortality due to massive and **nonspecific activation** of the immune system may be initiated by bacterial DNA and other products released from dying bacteria that reach concentrations sufficient to directly activate many lymphocytes. [Page 23, lines 33-36.]
an oligonucleotide delivery complex,	An "oligonucleotide delivery complex" shall mean an oligonucleotide associated with (e.g. ionically or covalently bound to; or encapsulated within) a targeting means (e.g. a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells). [Page 11, lines 10-13.] For administration in vivo, oligonucleotides may be associated with a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells to form an "oligonucleotide delivery complex". [Page 20, line 33-36.]
wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide	The instant invention is based on the finding that certain oligonucleotides containing unmethylated cytosine-guanine (CpG) dinucleotides activate lymphocytes as evidenced by in vitro and in vivo data. Based on this finding, the invention features, in one

	aspect, novel immunostimulatory oligonucleotide compositions. [Page 7, lines 7-10.] An "immunostimulatory oligonucleotide", "immunostimulatory CpG containing oligonucleotide", or "CpG ODN" refer to an oligonucleotide, which contains a cytosine, guanine dinucleotide sequence and stimulates (e.g. has a mitogenic effect) on vertebrate lymphocyte. [Page 10, lines 1-4.]
associated with a lipid or a sterol, wherein the lipid is a cationic lipid, virosome or liposome.	An "oligonucleotide delivery complex" shall mean an oligonucleotide associated with (e.g. ionically or covalently bound to; or encapsulated within) a targeting means (e.g. a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells). Examples of oligonucleotide delivery complexes include oligonucleotides associated with: a sterol (e.g. cholesterol), a lipid (e.g. a cationic lipid, virosome or liposome), or a target cell specific binding agent (e.g. a ligand recognized by target cell specific receptor). [Page 11, lines 10-16.] For administration in vivo, oligonucleotides may be associated with a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells to form an "oligonucleotide delivery complex". Oligonucleotides can be ionically, or covalently associated with appropriate molecules using techniques which are well known in the art. A variety of coupling or crosslinking agents can be used e.g. protein A, carbodiimide, and N-succinimidyl-3-(2-pyridyldithio) propionate (SPDP). Oligonucleotides can alternatively be encapsulated in liposomes or virosomes using well-known techniques. [Page 20, line 33, through page 21, line 2.]
53 and 66. wherein the non-specific immune response comprises stimulating natural killer	For use in therapy, an effective amount of an appropriate oligonucleotide alone or

(NK) cell activity.	formulated as an oligonucleotide delivery complex can be administered to a subject by any mode allowing the oligonucleotide to be taken up by the appropriate target cells (e.g. B-cells and NK cells). [Page 22, lines 9-12.]
54 and 67. wherein the CpG is not part of a palindromic sequence.	Disruption of the palindrome eliminated stimulation in octamer ODN (eg., ODN 4h), but palindromes were not required in longer ODN. [Page 13, lines 36-38.]
55 and 68. wherein the CpG includes a phosphate backbone modification.	Preferred stabilized oligonucleotides of the instant invention have a modified phosphate backbone. [Page 9, lines 28-29.]
56 and 69. wherein the phosphate backbone is a phosphorothioate backbone modification.	Especially preferred oligonucleotides have a phosphorothioate modified phosphate backbone (i.e. at least one of the phosphate oxygens is replaced by sulfur). [Page 9, lines 29-31.]
57 and 70. wherein the sterol is cholesterol.	Examples of oligonucleotide delivery complexes include oligonucleotides associated with: a sterol (e.g. cholesterol), a lipid (e.g. a cationic lipid, virosome or liposome), or a target cell specific binding agent (e.g. a ligand recognized by target cell specific receptor). [Page 11, lines 13-16.]
58 and 71. wherein the oligonucleotide is 8-100 nucleotides in length.	In a preferred embodiment, an immunostimulatory oligonucleotide is synthetic, between 2 to 100 base pairs in size . . . preferably in the range of 8 to 40 base pairs in size. [page 7, lines 12-22.]
59 and 72. wherein the oligonucleotide is 8-40 nucleotides in length.	In a preferred embodiment, an immunostimulatory oligonucleotide is synthetic, between 2 to 100 base pairs in size . . . preferably in the range of 8 to 40 base pairs in size. [page 7, lines 12-22.]
60 and 73. wherein the oligonucleotide comprises the formula 5' $X_1X_2CGX_3X_4$ 3' wherein C and G are unmethylated, X_1, X_2, X_3 and X_4 are nucleotides and a GCG trinucleotide sequence is not present at or near the 5' or 3' termini.	In a preferred embodiment, an immunostimulatory oligonucleotide . . . contains a consensus mitogenic CpG motif represented by the formula: 5' $X_1X_2CGX_3X_4$ 3' wherein C and G are unmethylated, X_1, X_2, X_3 and X_4 are nucleotides and a GCG trinucleotide sequence is not present at or near the 5' or 3' termini. [Page 7, lines 12-19.]
61 and 74. further comprising a	An oligonucleotide alone or as an

pharmaceutically acceptable carrier.	oligonucleotide delivery complex can be administered in conjunction with a pharmaceutically acceptable carrier. [Page 22, lines 17-18.]
62 and 75. wherein the oligonucleotide is encapsulated in the cationic liposome.	Examples of oligonucleotide delivery complexes include oligonucleotides associated with: a sterol (e.g. cholesterol), a lipid (e.g. a cationic lipid, virosome or liposome), or a target cell specific binding agent (e.g. a ligand recognized by target cell specific receptor). [Page 11, lines 13-16.] Oligonucleotides can alternatively be encapsulated in liposomes or virosomes using well-known techniques. [Page 21, lines 1-2.]
63 and 76. wherein the oligonucleotide is synthetic.	In a preferred embodiment, an immunostimulatory oligonucleotide is synthetic . . . . [Page 7, lines 12-19.]
64 and 77. wherein the composition activates a systemic, non-specific immune response when administered by an intravenous or intraperitoneal route.	For use in therapy, an effective amount of an appropriate oligonucleotide alone or formulated as an oligonucleotide delivery complex can be administered to a subject by any mode allowing the oligonucleotide to be taken up by the appropriate target cells (e.g. B-cells and NK cells). Preferred routes of administration include oral and transdermal (e.g. via a patch). Examples of other routes of administration include injection (subcutaneous, intravenous, parenteral, intraperitoneal, intrathecal, etc.). [Page 22, lines 9-14.]

§ 41.202(a)(6)

The following chart shows that claim 52 is supported by application Serial No. 08/276,358, filed July 15, 1994, entitling applicants to benefit of its filing date:

New Claim Number	Support in U.S.S.N. 08/276,358
52. A composition for activating	The instant invention is based on the finding that nonmethylated cytosine-guanine (CpG) dinucleotides activate lymphocytes (e.g. B cells and natural killer (NK) cells). [Page 4, lines 20-22.] In one aspect, the invention features method for activating lymphocytes (e.g. B cells and natural killer (NK) by contacting them with an oligonucleotide containing a non-methylated CpG. [Page 4, lines 30-32.]

non-specific immune response in a subject comprising:	The studies reported above indicate that oligonucleotides containing at least one non-methylated CpG dinucleotide can be directly mitogenic for lymphocytes (e.g. B cells and NK cells). [Page 14, lines 16-18.] This novel activation pathway provides a rapid **alternative to** T cell dependent antigen **specific** B cell activation. However, it is likely that B cell activation **would not be totally nonspecific**. [Page 14, line 35-37, (emphasis added).] Further, sepsis, which is characterized by high morbidity and mortality due to massive and **nonspecific activation** of the immune system may be initiated by bacterial DNA and other products released from dying bacteria that reach concentrations sufficient to directly activate many lymphocytes. [Page 23, lines 33-36.]
an oligonucleotide delivery complex,	An "oligonucleotide delivery complex" shall mean an oligonucleotide associated with (e.g. ionically or covalently bound to; or encapsulated within) a targeting means (e.g. a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells). [Page 6, lines 22-25.] For administration in vivo, oligonucleotides may be associated with a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells to form an "oligonucleotide delivery complex". [Page 13, line 26-30.]
wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide	The instant invention is based on the finding that nonmethylated cytosine-guanine (CpG) dinucleotides activate lymphocytes (e.g. B cells and natural killer (NK) cells). [Page 4, lines 20-22.]. Particularly preferred oligonucleotides for activating lymphocytes consist of a CpG . . . ." [Page 4, lines 24-26.]

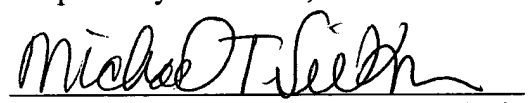
	These data confirmed that a CpG motif is the essential element present in ODN that activate B cells. [Page 8, lines 11-12.]
associated with a lipid or a sterol, wherein the lipid is a cationic lipid, virosome or liposome,	An "oligonucleotide delivery complex" shall mean an oligonucleotide associated with (e.g. ionically or covalently bound to; or encapsulated within) a targeting means (e.g. a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells). Examples of oligonucleotide delivery complexes include oligonucleotides associated with: a sterol (e.g. cholesterol), a lipid (e.g. a cationic lipid, virosome or liposome), or a target cell specific binding agent (e.g. a ligand recognized by target cell specific receptor). [Page 6, lines 22-28.] For administration in vivo, oligonucleotides may be associated with a molecule that results in higher affinity binding to target cell (e.g. B-cell and natural killer (NK) cell) surfaces and/or increased cellular uptake by target cells to form an "oligonucleotide delivery complex". Oligonucleotides can be ionically, or covalently associated with appropriate molecules using techniques which are well known in the art. A variety of coupling or crosslinking agents can be used e.g. protein A, carbodiimide, and N-succinimidyl-3-(2-pyridyldithio) propionate (SPDP). Oligonucleotides can alternatively be encapsulated in liposomes or virosomes using well-known techniques. [Page 13, lines 26-33.]
wherein the composition activates a non-specific immune response in the subject.	Activated lymphocytes, stimulated by the methods described herein . . . can boost a subject's immune response and therefore are useful for treating, preventing or ameliorating an immune system deficiency (e.g., a cancer or infection." [Page 4, lines 35-38.] This novel activation pathway provides a rapid **alternative to** T cell dependent antigen

	specific B cell activation. However, it is likely that B cell activation **would not be totally nonspecific**. [Page 14, line 35-37, through page 15, line 2 (emphasis added).] Further, sepsis, which is characterized by high morbidity and mortality due to massive and **nonspecific activation** of the immune system may be initiated by bacterial DNA and other products released from dying bacteria that reach concentrations sufficient to directly activate many lymphocytes. [Page 23, lines 33-36.]

Conclusion

If the Examiner and/or the Interference Practice Specialist has any questions regarding this paper, she is invited to contact the undersigned to expedite declaration of an interference.

Respectfully submitted,



Michael T. Siekman, Reg. No.: 36,276
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2211
Tel. No.: (617) 646-8000
Fax No.: (617) 646-8646

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